Katz, Martin 1995

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MARTIN M. KATZ

Interviewed by Jean Endicott
San Juan, Puerto Rico

December 14, 1995

JE: I'm Dr. Jean Endicott and I'm interviewing Dr. Martin Katz,*who's been a member of ACNP since 1963. Now, Dr. Katz, what field did you start out in?

MK: I got my basic education in chemistry, went into psychology in graduate school and received my degree in psychology at the University of Texas. So, I had an interest in these two disciplines for quite a while.

JE: How did you get into your current field?

MK: Into psychopharmacology?

JE: Right.

MK: After graduating from the University of Texas, I worked there for a year on research as a post-doctoral fellow. The project had to do with the effects of Vitamin C on intelligence, a study I was very skeptical would result in any positive results, but it was a nice position. I had run into Jonathan Cole at a scientific meeting in Texas, and he was impressed with the design of that study, because it was so much like a drug study. He was on the verge of taking over a large program at the National Institute of Mental Health on a new discipline called psychopharmacology, so he was seeking people who had done things like this or might be interested in that field. That was the last I saw of him for awhile. But shortly after completing that post-doc I went to Washington to work in the Veterans Administration Neuropsychiatric Laboratory. There I got involved in a project evaluating the outcome of psychotherapy and worked with Maurice Lorr, who was expert in development of quantitative rating scales for symptomatology. This is back in the late 1950s, and was a new research area at the time. And, I came across Dr. Cole there again. It turns out he was in charge of something like a two million dollar project by way the National Institute of Mental Health to promote this new discipline of psychopharmacology. All this happened because of excitement over the discovery of the new drugs for schizophrenia that was provoking a revolution in our field. They apparently couldn't give him enough money to get that program started. I was viewed as a young researcher, but I had the skills he was interested in. He was hiring people, so he brought me to NIH. I was recruited in 1957 as the Executive Secretary of the first Psychopharmacology Advisory Committee. I must have been thirty years old at the time and I was confronted with relating to all these senior scientists in the field from all over the country. So, it was a very exciting prospect.

JE: What was the reaction to having a psychologist head of that?

MK: I don't think there was any concern. These were the people going to put this new field so the committee was made up of representatives from several disciplines. Psychopharmacology, by definition, involved psychiatry, chemistry, pharmacology and psychology, so the mix of people involved was from all of these fields. They might come from whatever direction in the sciences. That was not unusual.

JE: What were some of the first programs you were involved in?

MK: The entity was called the Psychopharmacology Service Center (PSC) and the mission was to get out into the field and to develop this new discipline. That meant providing investigators with funds to develop programs in basic research on the new drugs and, in a parallel fashion, to attack the problems of clinically evaluating the new drugs. Despite knowing the drugs worked and, having seen them do so in small studies, they needed definitive evidence on large representative samples around the country that the drugs were effective. So, the second part of the program had to do with what they called Collaborative Multi-hospital Clinical Programs for the evaluation of these new drugs. To Jon Cole's credit he was able, with the help of his staff, to launch these studies. They were the first collaborative studies ever launched by NIMH to investigate this kind of issue, which is the evaluation of psychiatric treatments. So the Center staff had to be concerned about issues in both basic and in clinical research.

JE: Do you remember who some of the people in the field were back then?

MK: The Chairman of this advisory group was Ralph Gerard, a nationally known neurophysiologist from the University of Michigan. In psychology, it was Howard Hunt, Columbia University. In biology and psychiatry, it was Seymour Kety. Nathan Kline, a clinical researcher, was one of the real movers in the field; he helped generate the funds for the program. Louis Goodman, Chairman of Pharmacology at University of Utah, was the author of the most prominent text in clinical pharmacology. These were much respected people and they were, because of the funds and new opportunities, as excited as everybody else about this field.

JE: Could you tell us something about what your career was and what you did in relation to that?

MK: I was Executive Secretary, which meant active involvement in the review of grant applications and support of some research programs in my area of work. Then, after almost two years in that position, I went back into active research at the Center. I worked with the collaborative programs that had begun to develop methods of evaluation. I was given the task of developing a methodology for evaluating the long-term effects of these agents once the patients when they went back into the community; how long did the early positive effects last. That was a major issue and I developed a method for measuring clinical and social adjustment in the community. They were called the Katz Adjustment Scales and they're still in use. On an analogous issue there was short-term evaluation of the drugs. Having come out of the laboratory in the VA, I was very familiar with those techniques and helped put them together for that large-scale study. So, I worked on that part of the study and also on issues around psychedelic, LSD type drugs. These drugs were also a major issue. When the field started we had this parallel development of "good" drugs, the tranquilizers and antidepressants, the ones supposed to solve mental disorder, and "bad" drugs, the psychedelics. The latter were capable of disrupting the "personal psyche" and the whole community. I was given responsibility for following up on those drugs, accumulating scientific evidence on their actions and impact. After doing that for a few years, I was appointed head of a special studies section for psychopharmacology. It gave me the opportunity to develop a laboratory that would look more intensively at LSD type drugs. With a small staff I developed a laboratory in a prison to look at new methodologies for studying how they worked. At first, for safety, we experimented with small dosages to see the early psychological effects. Later we expanded these studies and managed to get a number of other investigators involved. So, this research grew into a major program, in parallel to what was going on in the community, with funds increasing every year. I was heavily involved from about 1963 until 1968. Then I was able to follow another interest I had, the influence of culture as a variable in drugs effects, and more generally as a factor in the expression of abnormal behavior.

JE: Expression of abnormal behavior?

MK: Right. Also, I got involved, by way of that special studies group, with the broader issue of classification of disorders. We mounted a very large national conference in 1965 that resulted in a book on *Classification of Mental Disorders* designed with Jonathan Cole and Walter Barton, who was head of the American Psychiatric Association. That national conference identified some of the major problems confronting the field with regard to diagnosis, which I would be involved in later.

JE: What were the drugs that you worked with, other than LSD? Were they mainly antipsychotics or were you, also, involved with the antidepressants?

MK: During the 1960's mainly antipsychotic drugs. I had done a lot of work on the phenomenology of schizophrenia, on the effects of drugs on schizophrenia, by way of the quantitative rating methods developed during that time. That was my main area of work. Then, in the studies with LSD we used amphetamine and chlorpromazine as controls. Those lines of research ran parallel, they didn't cross.

JE: Were you using videotape technology back then?

MK: No. I wasn't involved with that at that time.

JE: So, you moved into the issue of cultural expression and the response of different ethnic groups to treatment. Could you say something about the project?

MK: I spent 1968 at the University of Hawaii in Honolulu on a Fellowship from the Mental Health in Asia and the Pacific Program. I took some of the rating methods we'd developed for clinical drug trials to apply to the issue of whether psychosis in Hawaii-Japanese and Hawaii-Caucasian schizophrenic patients was expressed differently in symptoms and social behavior. Hawaii was a great laboratory for examining the effects of ethnic influence on behavior, so it was part of the reason I was sent there. We worked out a research program for doing that at the State hospital. We started research and I did get involved in videotaping about that time, because we were attracted to the possibility of demonstrating the differences in pathology in a more open way, so that people could see it more clearly than by just extracting information from the scales you and I are very familiar with. I was there for a year; greatly stimulated by the East-West Program on Mental Health in Asia and the Pacific. The NIMH, in the meantime, had changed structurally, under a new Director. Psychopharmacology became a branch. The new NIMH director was Stan Yolles, and they had redesigned how they were going to support research in the future. As part of the reorganization they created a new Clinical Research Branch and had a chief of it for about a year. He, however, ran into some difficulty and decided to leave. This was a new branch with a whole new mission. Lou Wienckowski, who was the director of the division of extramural programs, offered me the position of Chief of that branch which brought me back from Honolulu. That branch had a direct line to psychopharmacology; because what psychopharmacology had accomplished was to make us all aware we had to do a better job of evaluating treatments. It sounds very strange, and you'd think we were well equipped to do that kind of thing by then. But it was the sixties and there were very few people who had a strong psychometrics orientation or who were in a position to develop the kind of instruments capable of sound tests of whether one treatment was better than another. The kind of background I had made it easier for me to go into the general field of clinical research. Psychopharmacology still figured strongly but in clinical research proper we would have to look at the world differently. The broad field of clinical studies was partitioned into a program on depression, one on schizophrenia, a program on psychosocial treatments, a program on basic psychopathology and one on biological factors in mental disorder. After I became Chief of the Branch, we developed "focused programs," as for example, the program on depression and psychosocial treatments. Then we began programs in psychopharmacology that had thrusts in two directions. We had to promote and support investigators in the field who could develop methodologies we needed and also promote the general field of clinical research. To do that we had to stimulate the field by way of conferences and support of collaborative research. In many ways it was a direct extension of what we had been doing in psychopharmacology. I never left psychopharmacology as a specialization, I just extended my interest. I still came to the ACNP meeting every year, regardless.

JE: When you took over as head of the Clinical Research Branch, do you remember what the budget was?

MK: It must have been in the area of about five million dollars.

JE: And that was the period when it was growing fairly rapidly.

MK: By the time I left, which was ten years later, it was somewhere in the range of twenty to twenty-five million dollars, so, it had gone up rapidly during those years. Those were good days for mental health research. Psychopharmacology had a lot to do with stimulating support for all areas of our field and we appreciated that. In that ten-year period we had several stimulating conferences. In 1969 there was the well-known Williamsburg Conference, which highlighted depression and the very exciting work on neurochemical theories of depression, the so called catecholamine hypothesis of affective disorders identified depression as a derangement of central neurochemical systems. The work had grown out of psychopharmacology, because the discovery of antidepressants opened up the issue of how these drugs were working. The drugs appeared to be changing functioning in certain neurotransmitter systems and investigators were able to associate the changes with depression. It looked as if we were very close to learning what the biochemical source of the depressed condition was. But you couldn't arrive at a definitive answer unless you did clinical studies, which were sound methodologically, and had the proper breadth and reliable diagnostic information. So, it raised the question of how to achieve a clinical study with a sufficiently large and diverse sample to test the biochemical hypothesis. And the need for such a study was one of the conclusions of that conference. But, the real issues identified as important to resolve, before the field could go forward, were three. One was confusion over diagnosis. At that time, there were several diagnostic systems and people argued about them continuously. You couldn't compare the results from one study to another because of the different diagnostic systems they used. Out of that discussion came a recommendation that we develop a more reliable nosological system for research purposes. The second issue had to do with pursuing ideas about the genetic basis of the disorders, and the third had to with testing, in a definitive way, the exciting neurochemical hypotheses. From that meeting, where we had some of the best minds in the country, a set of recommendations were developed with the idea that we generate a collaborative study. But before that occurred, something had to be done about upgrading the methodology to be used, particularly for diagnosis. You might remember this very well because you were one of the key figures we turned to. After the meeting we asked Bob Spitzer and your group, with Eli Robins, from St. Louis to "collaborate" and clear up the methodology relevant to diagnosis.

JE: Believe it or not, we did.

MK: First we had to refine the "Research Diagnostic Criteria", because we wanted to have diagnoses that met research standards for reliability so that a clinician in Iowa wouldn't be collecting data in a different way than a clinician in New York. So you and your group were commissioned to develop a standardized data collection instrument. After getting that done, if we had stopped we would have accomplished a lot, because those instruments you, Bob Spitzer and Eli Robins developed, the RDC and SADS, have been used by almost all investigators for the past twenty years. It upgraded quality and helped make collaborative studies possible. Now we could proceed to test ideas about the neurochemistry of depression and the role of genetics. We organized another conference on the psychology of depression so we could better study the principal theories and psychological phenomena in depression. That also was a successful conference and was followed, as was the biological conference, by a published book. The title of the first book on the Williamsburg Conference, edited by Williams, Katz, and Shield was, *The Psychobiology of the Depressive Illnesses*; and the title of the second book, edited by Friedman and Katz was, *The Psychology of Depression*. Later on we attacked the whole issue of psychotherapy for depression and compared it directly with drug treatment through a collaborative study, published in an article by Waskow, et al. in the *Archives of General Psychiatry*. What I'd like to point out about those initial studies, The Clinical and the Biological Collaborative Studies on the *Psychobiology of Depression*, was that they were the first collaborative studies. There's a question now whether similar studies will ever get done, designed to test experimental hypotheses. At that time we were familiar with the type of collaborative study intended to evaluate a treatment. We had a format for that. But we never used the methodology for a study that would go beyond treatment to test theoretical hypotheses about the causes or nature of a major mental disorder.

JE: There were other differences, too. Most collaborative projects were designed in Washington and carried out across the country. And the way you set up these new programs, there was a lot of back and forth deciding what was going to be studied. Could you describe some of that?

MK: We would bring our group of scientists and clinicians, leaders in the field, together, and they would have responsibility for designing the study. We had the staff to help and people of substantive background at the NIMH who could collaborate in the design and the work, but their status in the group was as co-investigators. The group would design the project and participate in carrying it out. To use the Collaborative Biology Study as an example; we had the expert in neuroendocrinology at one center who would take care of the laboratory work for the six participating hospitals, whereas measures of central nervous system chemistry were handled in another laboratory. The investigators who ran each study were leaders in the field, people like Peter Stokes at Cornell and Jim Maas at Yale. In St. Louis, the group would be using the most advanced equipment, mass spectrophotometry, for measuring drug concentrations in the plasma. At that time, there were only two or three pieces of that type of equipment in the entire country. The St. Louis group and Eli Robins would take responsibility for that work. We would, in Washington, take responsibility for the behavioral analysis. It was in that biological study that we instituted the video method, so that we had a pictorial record, based on the standard interview you promoted earlier for data collection. Since these assessments would be done frequently in the drug evaluation process, we developed a much briefer, simpler interview for the video work. But every patient would get the same standard interview at each assessment point. We intended to create a psychological testing instrument out of this, a standardized instrument interview and rating procedure that would be administered pre, during and post the course of drug treatment. This was a new technique added to the standard instruments, the Hamilton scale and SADS-C. So, that's the way the biological component of the collaborative studies was conducted. Its parallel was the clinical study which investigated nosology and genetics, and had as complex a collaborative arrangement as the biological study, involving investigators from all over the country. We were quite proud of those studies. They had a lot of effect on research if you examine its impact on the scientific community, apart from the study's actual results. In a sense, the collaborative network and studies served as mechanisms for psychiatric and research training in our field. While we didn't have that many centers in the country, they could train a large number of investigators. The field was still young at that time and we like to think that people like you, Nancy Andreasen, Paula Clayton, Bill Coryell, Martin Keller, Jim Kocsis, Alan Swann, Regina Casper and Steve Secunda could go on to be leading investigators in our field. So that was a major plus for the program in a field that needed improvement in the quality of its methodology to solve the major clinical and scientific problems that confronted us.

JE: You also had skeptics who thought that it was going to be impossible for groups of independent investigators to work in a collaborative fashion. But the fact is those programs are still running.

MK: That's right. We were thinking about that at the recent memorial for Gerry Klerman, Chairman of the clinical study. Unfortunately, we also lost Jim Maas who was the moving force behind the whole biological effort. In the talks at Gerry's memorial, we realized that the leaders of these two groups had to be strong people to manage investigators who were independent leaders in their own right. The co-investigators were all very accomplished and they weren't used to working closely together with other people, who they viewed more as competitors than collaborators. So the strong leadership qualities that were necessary in a Chairman were certainly fulfilled by Gerry Klerman and Jim Maas.

JE: That was planned, on your part, carefully.

MK: You make a lot of mistakes, but in those cases we chose well. You and I know that the clinical study wouldn't have lasted three or four years if we didn't have somebody like Gerry at the helm. I feel the same way about Jim Maas who was at the helm on the biological aspects of the study.

JE: You were chief of the Clinical Research Branch of NIMH during that time.

MK: As Clinical Research Branch Chief, over that ten-year period, there was another accomplishment we were proud of. Toward the end of that tour, we managed to establish the Clinical Research Center Program. This was a kind of program the NIH supported for almost all medical specialties but we did not have one in mental health in the early 1980's. A lot of people were very skeptical about it being a worthwhile venture. It seemed it would require large amounts of money for very broad programs of research and training when the NIMH was used to putting money in very specific, focused research programs. The latter could be monitored more easily, more effectively. But we also knew the side effects of creating these unusual programs where we were in great need of trained investigators. We needed people to have more room to develop so those centers would be a little more expensive, but we would get a lot more people into the field and a lot more problems solved. And it did work that way. I understand it is now being phased out, but I think it did great service for the development of our clinical research program for the past twenty years.

JE: I hope it's not over.

MK: I think it's close to being over because of budget constraints.

JE: What have you seen as major changes over the past twenty years in your work and contact with people?

MK: That's a difficult question but you can look at it from the standpoint of what hoped might be accomplished and what has actually happened. When we look back over the field, we see that by the early sixties, almost all the major drugs we have today had already been developed. The class of tranquilizers for schizophrenia, the class of antidepressants for depressive and anxiety disorders, lithium for mania and maintenance of bipolar depressions were all available. These were revolutionary developments. Previously there had been very little effective treatment for schizophrenia and we were losing hope. Regarding depression, we were very skeptical in this country that the disorder had anything to do with biology. It was viewed as the most psychological of our illnesses and, suddenly, these chemical agents came along and appeared to resolve in a matter of a few weeks, a condition that previously lasted a year or two. Even the psychologists, the skeptics like us, who came from the other side of this theoretical controversy, were convinced that this as a real impact. Those were major developments. The expectations were very high, that we were on the verge of getting to the sources of mental disorder, their biological basis. We began to think they were all biologically based and it would just be a matter of time until we understood how all the drugs worked. That was because all of the effective drugs were discovered accidentally but we would now be designing and creating new drugs which would be more effective, faster and so forth. We thought all of these new developments were around the corner; we would just stoke the furnace a little, put more money in the field and get it done. And, as the field mushroomed, there were many more investigators, and much more money for development. If you look over the past thirty years, a lot has happened; plenty of drugs appear somewhat better, but until the introduction of Prozac (fluoxetine) in the early 1980's, nothing really remarkable happened. Now, some people feel these newer drugs are remarkable and I can go along with part of that, but I don' t think it's the kind of development we saw with the first wave of new drugs. That's a long time between breakthroughs. Secondly, we thought that the roots of mental disorder would be uncovered and we would be able to link biological variables to mental disorder directly. In other words we would have "biological markers" for the disorders to an extent that when a patient walked into an interviewing or examination room and had blood taken there would be a test to tell us if this patient was schizophrenic or depressed. That hasn't happened. Not only hasn't it happened, we have yet to find a biological marker for any mental disorder that can be used in a diagnostic or predictive sense. Thirdly, the mechanisms of action underlying how these drugs bring about recovery are still clouded. The theories are very interesting, but we don't have definitive answers and it may be the reason we have not been able to develop new, revolutionary, drugs. On the other hand, a great deal has happened. We have struggled with these issues in the biological study of depression over many years. We're disappointed in a lot of what we were not able to find. On the other hand, we have found a few things through our work. The idea that antidepressant drugs don't impact the illness until two or three weeks pass, that widely accepted notion, is not quite true. We found that a lot goes on in the beginning that wasn't measured. The assumption of a delay is based on the fact that the drug didn't change depression as a whole without acknowledging that it did change aspects of the syndrome, for example the anxiety or anger level, very early. That may sound a small thing to make a great deal of. When investigators felt nothing happened for two or three weeks, they moved away from the notion early actions of the drug on neurochemistry were the key to antidepressant effects. So, they started to look later in the treatment process, opening up a whole new field of inquiry. We feel they abandoned, too quickly, looking at the initial stage of neurochemical changes. A lot of this controversy comes about because of the diminished role measurement of behavior has played. For some reason, behavior receded into the background with the introduction of all this exciting biological methodology. The fact that you could get a new discipline like molecular biology or neuroimaging applied to our field raised the excitement level so much that the whole area of behavior has been neglected. Jim Maas and I worked very hard on trying to conceptualize this state of affairs that led to misdirection. We made the point that drugs don't work specifically on a disorder. That isn't part of the drug language. The language of the drug is to affect certain systems in the body, which result in changes in behavior that are specific and are going to get related to mental disorder. But the issue really is relating changes in neurochemical functioning to specific actions on behavior. We argued for trying to think in terms of neurochemical components in the action of drugs, rather than in terms of their action on disorders and diagnoses. But if we go to the trouble to get down to such refined intricate biological measurements we should be doing the same thing in the sphere of behavior.

JE: Phenomenologically.

MK: Right, if we want to solve that problem.

JE: So, where do you think we're going?

MK: We've all gotten a lift from the fact that studies that went on for thirty years to do with measuring neurotransmitter metabolites in CSF or urine or plasma, were all attempts to measure what's going on in the brain indirectly. It was very difficult work and it made some progress. But the real steps will be taken when we can measure brain functioning directly. With all the advances we should expect to see a little more rapid movement now. It appears to be moving along a little bit faster. If the behavioral side can be handled better in the future, by utilizing experts who can do this work carefully, we'll be able to connect up a lot more quickly in the future. What we want to know about the source of mental disorder is how does it come about? We have to acknowledge that although we have thousands of research articles we haven't quite got there yet. We know very little about the biology of the disorders and that's the big issue. The other big issue is how these drugs work, because the future rests on whether we can resolve that question. If we can understand how they work, knowledge will move in two directions, in one direction it will tell us more about the key facets underlying a disorder. That was the great hope. And in the other it'll allow us to use this behavioral compartmental model that's been available for ten or twenty years, to target transmitter systems. As we'll be able to do that more efficiently and more successfully, we'll be able to manipulate behavior much more easily. I do want to say something about one of the disappointments of the last thirty years and that is about the "bad" drugs, the LSD-type drugs I spoke of in the beginning. . Those who remember that era, recall what a wild era it was. From the standpoint of NIMH, we used to have people come to see us, perfectly sound, established investigators, who had ideas of putting these drugs into the water of Jack Kennedy and Kruschev to bring peace in the future and so forth. They had seen the light. Of course we worked with these people, because there had been wild ideas before and some worked. But this movement frightened the field and, in the course of it, we left these drugs rather early. There's not much we could have done about that, because they were potentially very harmful. But anyone who saw the impact these drugs had on the mind, from a psychological point of view, had to feel we were knocking on the door of a better understanding of what goes on in the brain. These drugs produced remarkable changes in ideas, perceptions, and images, given in a dosage almost invisible to the naked eye. Yet, somehow, we couldn't quite get a grasp on them that would allow us to learn enough to move on in a way that would have an effect on science. We watched the drugs get buried under an avalanche of bad publicity and bad effects. Not that we could afford to let their indiscriminate use go on, knowing how much damage they can bring about. But drugs that have that kind of power should not have been abandoned. I'd say that is another lost venture.

JE: A kind of a missed opportunity.MK: We have, in some way to be able to open that door again, without losing control of the potentially harmful things associated with it.

JE: Were there other points you wanted to make about the history and your role?

MK: I'd just like to say that I consider myself very lucky that through a fortuitous set of events I wound up in that job at the PSC at such a young age and got to see so much of what was going on in the country and the world. I was in a favored position for many years to watch this whole field of neuropsychopharmacology develop. When I left after a span of time in psychopharmacology and clinical research, I became a Professor at Albert Einstein College of Medicine for ten years. I tried to develop a new program in psychology that would take advantage of the different ideas from the different disciplines I came across. But this is an era in which everything seems to be to be more constrained, pulling back, so we've got to be patient and maybe it will open up again at some point. That's the story.

JE: Thank you.

End of Interview

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* Martin M. Katz was born in New York City, New York in 1927.